III. REMARKS

The undersigned gratefully acknowledges the courtesies extended by Examiner Fubara during the interview conducted on June 27, 2003. During the interview, all of the pending claims were discussed. Also during the interview, Scott (U.S. Patent No. 3,621,097) and Timmons et al. (U.S. Patent No. 6,475,521) were discussed.

Reconsideration of this application in view of the following remarks is respectfully requested. Claims 1-4, 6-20 and 24-36 (including new claims 35 and 36) are pending.

In the Office Action, the Examiner rejected claims 1-4 and 30 under 35 U.S.C. §112 second paragraph, the Examiner noting that the limitation "said antihyperglycemic drug" in line 3 of claim 1 lacks anticedent bases. As discussed during the interview, this informality has now been corrected by the present amendment.

During the interview, the undersigned brought to the Examiner's attention the fact that U.S. Patent No. 6,475,521 (Timmins et al.), previously made a record in this case, has an original filing date of March 19, 1998. On the other hand, the undersigned advised the Examiner that the filing date of the parent case to the present application was March 20, 1998. Therefore, this reference, which is assigned to Bristol-Myers Squibb Co. and which may be directed to a commercially available product (Glucophage® XR (metformin hydrochloride extended-release tablets)) would be available as prior art to the present application by 1 day under 35 U.S.C. §102(e). However, during the interview, the Examiner was advised that the Timmins patent would be eliminated as prior art under 35 U.S.C. §102(e) by virtue of a declaration filed under 37 CFR 1.131.

Accordingly, enclosed herewith as Exhibit A is the declaration of Xiu Xiu Cheng under 37 CFR 1.131 that proves that the invention of the claim subject matter by the applicants occurred prior to the effective date of the Timmins reference. It is respectfully submitted that the

Cheng declaration eliminates the Timmins reference as prior art which is available to the Examiner. It is further noted that the commercially available product, Glucophage® XR was not commercially available as of the priority date of the present application.

In the Office Action, claims 1-4, 6-20 and 24-34 were rejected under 35 U.S.C. §103(a) as being as being unpatentable over Scott (US 3,621,097).

As noted by the Examiner, Scott describes a method for treating mental illness comprising administration of a composition that comprises dimethyl biguanide (metformin).

As discussed during the interview, the undersigned respectfully submits that the Scott reference is directed to the administration of dimethyl biguanide to an animal receiving an ataractic. Indeed, the entire specification of the Scott reference acknowledges that although dimethyl biguanide is a known hypoglycemic agent, it is being used therein to treat mental illness due to its alleged potentiating affects on ataractics. (See, e.g., column 4, lines 38-40 of Scott).

The Examiner takes the position that Scott suggests formulating a sustained-release dosage form. Indeed, it was noted that during the interview that the specification mentioned that the "compounds can be prepared for oral administration in the form of simple or sustained-release tablets . . . ." (Column 4, lines 31-37). The Examiner takes the position that it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare the formulation of Scott as sustained-release dosage form because Scott suggest formulating as a sustained-release dosage form. However, the Examiner has relied upon no other reference to make this rejection. Scott itself is completely lacking in any direction concerning how one would make a controlled-release metformin formulation. It is respectfully submitted that the Scott's disclosure will not suffice as prior art because it is not enabling in of itself. *See Paper List Accounting, Inc. v. Bay Area Rapid Transit System*, 231 USPQ 649 (CAFC 1986), citing in *Ray Borst*, 145 USPQ554, 557 (CCPA 1965), *cert. denied,* 382 US973 (1966). It was further

noted that at the time that the Scott reference was written, sustained-release formulations were not common place, and were not enabled.

During the interview, the undersigned further pointed out to the Examiner that Scott was limited to the treatment of mental illness. The undersigned noted that pending claims 33 and 34 were directed to an addition aspect of the present invention, that controlled-release oral dosage forms presently claimed when administered in the presence of food do not provide a decrease in bioavailability of metformin relative to administration of the same dosage form in the fasted state, or exhibit an increase in the bioavailability of the metformin from the dosage form as compared to the fasted state.

In the Office Action, the Examiner at page 3 took the position that the influence of food on the bioavailability of the metformin is a property of metformin. However, during the interview, it was pointed out that this is not a property of the drug itself. In support of applicants' position, a copy of the PDR section on the brand name immediate release metformin product, Glucophage® was shown to the Examiner. Therein, at page 1080, right column, it is stated that "food decreases the extent of and slightly delays the absorption of metformin, as shown by approximately a 40% lower mean peak concentration (Cmax), a 25% lower area under the plasma concentration versus time curve (AUC) and a 35 minute prolongation of time to peak plasma concentration (Tmax) following administration of a single 850 mg tablet of metformin with food, compared to the same tablet strength administered fasting." A copy of this section of the PDR is enclosed as Exhibit B to this amendment.

It is respectfully submitted that Exhibit B demonstrates that the bioavailability property of the claim controlled-release dosage form when administered with food are not a property of the drug itself, and that the Examiner's rejection on that basis should be removed.

Finally, with respect to claims 33 and 34, these claims are directed to a method of treating a human with an oral solid dosage form of metformin administered in the presence of food.

During the interview, the possibility that these claims would be amended to specify that the method was directed to the treatment of human diabetic patients, and that the administration step would be limited to a human diabetic patient. By virtue of the present amendment, this change has been made. Further, new claims 35-36 have been added (directed to a once-a-day administration).

During the interview, the Examiner agreed to separately consider the patentability of the method claims in view of the presently made differentiation over the Scott reference.

IV. Conclusion

It is respectfully submitted that in view of the actions taken an arguments presented, that this case is now in condition for allowance. An early and favorable action on the merits is earnestly solicited.

According to currently recommended Patent Office policy the Examiner is specifically authorized to contact the undersigned in the event that a telephonic interview will advance the prosecution of this application.

Respectfully submitted,
DAVIDSON, DAVIDSON & KAPPEL, LLC

By: _____
Clifford M. Davidson
Reg. No. 32,728

Davidson, Davidson & Kappel, LLC
485 Seventh Avenue, 14th Floor
New York, New York 10018
(212) 736-1940